

# A case cluster of possible tissue invasive gonorrhoea

M G Brook, S Clark, A Stirland, M C Kelsey, E W Paice, P D Kell, W A Atia

## Abstract

**Objective**—To describe a cluster of patients presenting with severe symptoms and infected with an unusual strain of *Neisseria gonorrhoeae*.

**Setting**—A north London Department of Sexual Health.

**Patients**—Five patients were linked by reported sexual contact or other epidemiological evidence as part of a cluster of gonococcal infection. Cultured *N gonorrhoea* were subtyped by serological (serovar) and cultural (auxotype) methods and antibiotic sensitivities measured by minimum inhibitory concentration (MIC).

**Results**—Four of the patients had severe gonorrhoea-related systemic or extra-genital symptoms: disseminated gonococcal infection with oligoarthritis (1 patient), acute pelvic inflammatory disease (1 patient, who was also chlamydia positive) and tender inguinal adenopathy (2 patients). The fifth patient was asymptomatic. *N gonorrhoeae* was isolated in four of the patients. All four organisms had identical MICs. Three of the organisms were subtyped and found to be the same rare strain (serovar 1A1, auxotype NR).

**Conclusion**—This case cluster provides evidence for strain-related virulence in an uncommon gonococcal subtype.

(Genitourin Med 1995;71:126-128)

Keywords: Gonorrhoea; Auxotype; Serovar

## Introduction

There is evidence that invasive gonococcal disease is a function of both host factors, such as deficiencies of late stage complement factors or immunity from previous exposure,<sup>1,2</sup> and inherent increased pathogenicity of certain organisms, associated with their serotype and auxotype (nutrient requirements).<sup>3,4</sup> Information on the pathogenicity of micro-organisms can be gained from both population studies and investigation of outbreaks. Current data relating gonococcal sub-types with their pathogenic potential have come mainly from cross-sectional studies of genitourinary medicine clinic attenders.<sup>3-5</sup> There is little published information tracking individual virulent strains as part of a cluster.

## The outbreak (fig 1)

**Case 1** A 36 year old woman was referred from the rheumatology department on 28 January with a two week history of arthritis involving the left wrist and knee, fevers and a mouth ulcer. Cervical and urethral swabs taken at this visit grew *N gonorrhoeae* but a joint aspirate was sterile. A clinical diagnosis of gonococcal arthritis and disseminated gonococcal infection was made whereupon she was treated with amoxycillin (3 g stat, then 500 mg qds for 10 days) and probenecid (1 g stat, then 500 mg qds for 10 days) in addition to ibuprofen. A cervical swab for chlamydia, vaginal swab for trichomonas and blood test for syphilis were negative. She would not identify her sexual contacts.

**Case 2** On 11 February a 25 year old woman was referred by her general practitioner complaining of dysuria for ten days and fever with a right-sided tender inguinal swelling for two days. A urine culture taken by her GP was negative. She had received empirical trimethoprim for 3 days and penicillin V for 1 day prior to attending this clinic. Examination confirmed a tender enlarged right inguinal lymph node 2 cm in diameter with no obvious cause. In particular there was no evidence of herpes. A full set of genital tract swabs (microscopy and culture) for chlamydia, gonorrhoea, trichomoniasis and herpes was negative.

**Case 3** On 15 February a 21 year old man was seen for an STD screen being a sexual contact of case 2. The patient reported unprotected sex on one occasion three days prior to the onset of case 2's illness. He lived close to case 1. Case 3 was asymptomatic but *N gonorrhoeae* was identified on microscopy and culture of a urethral swab. Tests for chlamydia

Archway Sexual Health Clinic, Camden and Islington Community Health Services NHS Trust

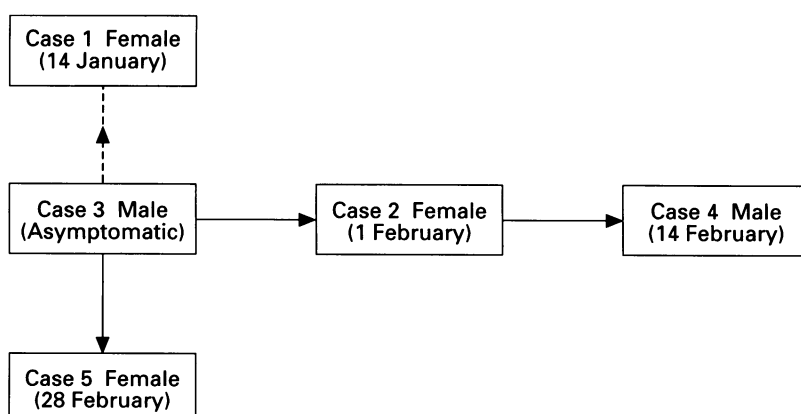
M G Brook  
A Stirland  
P D Kell  
W A Atia

Department of Microbiology, Whittington Hospital NHS Trust, Highgate Hill, London N19 5NF, UK

S Clark  
M C Kelsey

Department of Rheumatology  
E W Paice

Correspondence to: Dr M G Brook.



Relationships of the five cases based on the epidemiological and microbiological data. Dates in brackets indicate onset of symptoms, arrows indicate probable route of transmission, solid lines show confirmed sexual contact and broken line suspected sexual contact. All except case 1 report sexual contact with the respective partners within the incubation period for gonorrhoea.

and syphilis were negative. Case 2 and Case 3 both received amoxycillin 3 g and probenecid 1 g stat and doxycycline 100 mg bd for 7 days.

**Case 4** A 20 year old man was seen on 16 February complaining of dysuria and tender swelling of the left groin for two days and urethral discharge for one day. He named case 2 as his only sexual contact, with whom he had been having regular unprotected vaginal sex for one year, the last occasion being one day previously. He was found to have a purulent urethral discharge and bilateral enlarged tender inguinal lymph nodes. *N gonorrhoeae* was identified in the urethra on microscopy and culture, which was successfully eradicated with amoxycillin and doxycycline as above.

**Case 5** was a 25 year old woman who was seen on 7 March and complained of nausea, dizziness, and bilateral lower abdominal pain for one week. She had been having unprotected vaginal intercourse for two months with case 3, her only sexual contact. On examination she had a purulent green cervical discharge and marked tenderness in the vaginal fornices and on cervical excitation, typical of acute pelvic inflammatory disease. *N gonorrhoeae* was seen and cultured from the cervix and urethra, but she also had a positive chlamydia antigen swab from the cervix. She was given a single dose of amoxycillin and probenecid as above, followed by doxycycline (100 mg bd) and metronidazole (400 mg bd) for two weeks.

#### Microbiology

The isolates of *N gonorrhoeae* in cases 1, 3 and 4 were sub-typed (PHLS Gonococcus Reference Unit, Bristol) and found to be identical: Auxotype NR (non-requiring), Serovar IA1, with identical antibiotic Minimum Inhibitory Concentrations (fully sensitive to all tested antibiotics except moderate penicillin sensitivity (0.16 mg/ml)). The organism from case 5 was lost before subtyping could be carried out, but it showed an antibiotic sensitivity pattern identical to the three other organisms.

#### Discussion

This report is of interest for two reasons. Firstly it describes the passage of an organism of unusual virulence between five people, four of whom displayed more severe symptoms than usual: oligoarthritis, tender inguinal adenopathy (two patients) and pelvic inflammatory disease. Secondly, the organism (serovar IA1, auxotype NR) is unusual in this part of Britain with only 4 of 3800 consecutive strains at St Mary's Hospital Medical School, London being of this subtype (Dr CA Ison, personal communication) and it has only uncommonly been associated with more invasive disease.<sup>3</sup>

Combining epidemiological and microbiological data, there is strong evidence that all five patients were infected with the same organism. The most likely explanation of events being that case 3, the asymptomatic

gonococcus carrier, infected cases 1, 2 and 5 and case 4 was subsequently infected by case 2. Although the organism was not isolated in case 2 because of previous antibiotic use there can be little doubt that *N gonorrhoeae* was the cause of her symptoms from the epidemiological information that suggests acquisition of infection from case 3 and subsequent transmission to case 4.

Arthritis, as part of the syndrome of disseminated gonococcal infection, is uncommon, arising in about 0.5% of all infected patients and may be sterile or pyogenic.<sup>6</sup> The proportion of female patients with gonorrhoea who develop pelvic inflammatory disease is less clear, being reported as falling within the range 0.5 to 20%.<sup>6</sup> There is also a lack of precise data on the incidence of tender, enlarged inguinal adenopathy in men. Although Akers describes a 40% incidence,<sup>7</sup> it is certainly very unusual in the experience of ourselves and others.<sup>1,6</sup> Dahl and Dans describe biopsy of a lymph-node in such a case from which *N gonorrhoeae* was isolated,<sup>8</sup> which suggests that at least some cases are due to extra-genital spread of infection. We were unable to find any reference to tender inguinal adenopathy as a feature of gonorrhoea in women. It is therefore apparent that the combination of clinical presentations described in this cluster was more severe than average and suggests increased pathogenicity in this particular strain of gonococcus.

In previous studies using serotyping and auxotyping a wide range of gonococcus subtypes have been isolated from patients with invasive disease.<sup>3,4</sup> It is clear that factors separate from the serotype or auxotype are responsible for pathogenicity. However, there is an increased incidence in the 1A serogroup, particularly 1A1 and 1A2 serovars and the AHU<sup>-</sup> (arginine, hypoxanthine, uracil requiring) auxotype amongst invasive strains.<sup>3,4</sup> In the United States Knapp *et al*<sup>9</sup> found a very low incidence of the 1A1/2-NR subtype at a rate similar to that found in London by Ison. Morello and Bohnoff in Chicago also report that 1A1-non-AHU<sup>-</sup> subtypes were rare, but when found were significantly associated with invasion, although the NR auxotype was not mentioned specifically.<sup>3</sup>

Paradoxically, one of our cases was asymptomatic. This may relate to immunity following previous exposure.<sup>2</sup> However, the tissue-invasive AHU<sup>-</sup> gonococcal auxotype is also carried asymptotically more frequently than other auxotypes.<sup>10</sup> One might therefore speculate that some tissue-invasive strains are inherently less likely to cause urethritis.

This report has provided evidence of the increased pathogenic potential in a specific *N gonorrhoeae* subtype by describing the clinical course of infection in a group of five epidemiologically related patients. It adds further weight to the argument that variations in disease manifestation may be organism-related although more precise tests are required to define the factors influencing pathogenicity.

Serotyping and auxotyping was performed by Dr A Turner, Gonococcus Reference Unit, Bristol.

- 1 Petersen BH, Lee TJ, Snyderman R. *Neisseria meningitidis* and *Neisseria gonorrhoeae* bacteremia associated with C6, C7 or C8 deficiency. *Ann Intern Med* 1979;90:912-20.
- 2 Plummer FA, Simonsen JN, Chubb H, et al. Epidemiologic evidence for the development of serovar-specific immunity after gonococcal infection. *J Clin Invest* 1989;83:1472-6.
- 3 Morello JA, Bohnhoff M. Serovars and serum resistance of *Neisseria gonorrhoeae* from disseminated and uncomplicated infections. *J Infect Dis* 1989;160:1012-7.
- 4 Tapsall JW, Phillips EA, Schultz TR, Way B, Withnall K. Strain characteristics and antibiotic susceptibility of isolates of *Neisseria gonorrhoeae* causing disseminated gonococcal infection in Australia. *Int J STD Aids* 1992;3:273-7.
- 5 Ross JDC, Wardropper A, Sprott M, Moyes A, Young H. Gonococcal infection in Edinburgh and Newcastle: serovar prevalence in relation to clinical features and sexual orientation. *Genitourin Med* 1994;70:35-9.
- 6 Morton RS. *Gonorrhoea*. London: WB Saunders, 1977.
- 7 Akers WA. Tender inguinal lymph nodes and gonococcal urethritis. *Military Med* 1972;137:107-8.
- 8 Dahl R, Dans PE. Gonococcal lymphadenitis. *Arch Int Med* 1974;134:1116-7.
- 9 Knapp JS, Holmes KK, Bonin P, Hook EW. Epidemiology of gonorrhea: distribution and temporal changes in auxotype/serovar classes of *Neisseria gonorrhoeae*. *Sex Trans Dis* 1987;14:26-32.
- 10 Crawford G, Knapp JS, Hale J, Holmes KK. Asymptomatic gonorrhea in men: caused by gonococci with unique nutritional requirements. *Science* 1977;196:1352-3.